

# Life & Times

## Syphilis and Salvarsan

The progress of medical science is often written as if Western scientists brought effective cures into the modern world. The story of Salvarsan, the first modern scientific treatment for syphilis, shows a different story; one of exchange between Europe and Japan.

Syphilis appeared as a new disease in Europe and Asia in the 15th century (Europe in 1495, in Japan in 1512). Over its first centuries syphilis changed from a very aggressive disease with a high early mortality to the more indolent disease we know today and which may have affected 10% of the population in England at the end of the 19th century.<sup>1</sup> It was the AIDS epidemic of its day.

### THE JAPANESE CONNECTION

The Swedish botanist Carl Thunberg (1743–1828) believed that he was the first person to supply a modern treatment for syphilis to the Japanese. He was a disciple of the botanist Carl Linnaeus and one of the very few European botanists to gain some access to Japan during the Tokugawa period (1603–1868) when it was closed to Westerners. On his return he compiled a *Flora Japonica* which was acknowledged by both Europeans and Japanese as a significant advance in their botanical knowledge. European visitors of Thunberg's time, however, did not have the feelings of superiority to Japanese culture that would typify their 19th century successors; Edo (Tokyo) was a city of a million people, bigger than any town in his native Sweden.<sup>2</sup>

Thunberg's contacts with the native Japanese people was limited by the Japanese government to the interpreters in Dejima, the island where foreign visitors had to stay. These interpreters' posts were held by families over several generations and the role had a low status in Japan. As well as the interpreting, they worked as doctors and taught medicine; belonging to the 'Rangaku' school which looked to the West. To some of them Thunberg taught

the mercury treatment of syphilis then used in Europe. Yoshio Kosaku, one of his Japanese students, then further developed this formula. Thunberg believed that he had taught them an efficacious treatment and that this was a fair exchange for the many botanical specimens they had collected for him. But he was wrong on two counts. First, we do not now think that mercury is an efficacious treatment for syphilis. Second, mercury treatment was already widely known and practised in Japan, but by a different school of doctors with a higher social status; those who had studied Chinese medicine. A book describing the mercury treatment of syphilis had been published in Japan by this group of doctors in 1725, long before Thunberg reached Japan.<sup>3,4</sup>

### FINDING A 'MAGIC BULLET' FOR SYPHILIS

Now for Salvarsan; recognised as the first scientific and effective cure for syphilis. It was discovered by a Japanese man; Professor Sahachiro Hata. Admittedly, this was again in the context of a cultural exchange; between the Japanese and German empires on this occasion. The Japanese had opened to the world since 1854 and were now sending 16 graduates a year to prestigious German universities. Sahachiro Hata had already done good work in Japan researching bubonic plague with Kitasato, Shibasaburo (the co-discoverer of *Yersinia pestis*). He was sent to Ehrlich in Frankfurt. Paul Ehrlich, the German-Jewish student from Breslau (now known as Wrocław, Poland) who had made his way to the heart of the German medical establishment, was running a programme to find a 'magic bullet' for syphilis. He was testing compounds synthesised by the chemist Alfred Berthelm. Sahachiro Hata was given compound 606 to test (the sixth of the sixth series). He set up a rabbit model of syphilis and found the compound effective in vivo. Human experiments followed. Some Salvarsan was sent by Ehrlich to his

colleague Neisser in Breslau, with whom he had shared a secondary school bench.<sup>5</sup> Neisser published a very positive report in the leading medical journal of the day.<sup>6</sup>

### NOBEL PRIZES

Soon Salvarsan was widely used. It remained a toxic organoarsenic compound, difficult to handle, with a great tendency to 'burn up veins', but it rapidly superseded mercury. Salvarsan and similar compounds remained the treatment choice for syphilis until penicillin, with its much lower toxicity, appeared after WWII.

Ehrlich was granted a Nobel prize in 1908. Sahachiro Hata received three, unsuccessful, nominations for a Nobel prize, one by Kocher, the Swiss thyroid surgeon and two by Japanese colleagues. Hata returned to Japan where he became the leading Japanese microbiologist of his generation.

To summarise, finding the cure for syphilis took several centuries. The Japanese played an active and, in the person of Sahachiro Hata, an essential part.

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